EXHIBIT 7

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Single agent thalidomide in patients with relapsed or refractory acute myeloid leukaemia

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Summary. Thalidomide is a putative anti-angiogenesis agent that has significant anti-tumour activity in haematological malignancies with increased bone marrow angiogenesis, including multiple myeloma (MM) and myelodysplastic syndromes (MDS). Increased levels of the mitogen for angiogenesis, vascular endothelial growth factor (VEGF), correlate with worse survival in acute myeloid leukaemia (AML). A phase II trial of thalidomide was conducted in patients with relapsed- or refractory-AML previously treated with cytarabine-containing regimens. A total of 16 patients with refractory- or relapsed-AML were treated with thalidomide 200–800 mg orally daily (median dose 400 mg daily) for a median of 27 d (range, 3–94 d). Overall, one patient (6%) achieved complete remission (CR) lasting for 36 months, and two patients had a transient reduction in marrow blasts from 8% and 7% to less than 5% in both cases. There was no correlation between reduction in levels of angiogenesis markers and response. Toxicities related to thalidomide were significant, and precluded dose escalation beyond 400 mg orally daily in most patients. Although there appears to be some evidence of biological activity, single agent thalidomide is not an optimal choice of therapy for salvaging patients with relapsed- or refractory-AML. Thalidomide analogues with more potent immunomodulatory activities and more favourable toxicity profiles may offer more promise as anti-AML therapy.

Keywords: thalidomide, acute myeloid leukaemia, relapsed acute myeloid leukaemia, refractory acute myeloid leukaemia.

Fiedler *et al* (1997) initially reported the presence of vascular endothelial growth factor (VEGF) transcripts and its receptors in leukaemia cells from patients with acute myeloid leukaemia (AML). Elevated levels of intracellular VEGF are independently associated with worse survival in patients with AML (Aguayo *et al*, 1999, 2000). These data provide a presumptive basis for anti-angiogenic therapy in AML (Giles, 2001, 2002).

D'Amato *et al* (1994) demonstrated that thalidomide inhibited basic fibroblast growth factor (bFGF)-induced angiogenesis in a rabbit cornea micropocket assay. Other investigators showed that the drug inhibited VEGF in a murine model of corneal vascularization (Kenyon *et al*, 1997). Efficacy with thalidomide has been demonstrated in multiple myeloma (MM) and myelodysplastic syndromes (MDS), entities where angiogenesis also appears to have an important role in the pathogenesis of the disease (Singhal *et al*, 1999; Thomas & Kantarjian, 2000; Raza *et al*, 2001; Thomas *et al*, 2001).

Recently, Steins *et al* (2002) reported encouraging results with single agent thalidomide in *de novo* and previously treated AML. Thus, we reviewed our historical experience with single agent thalidomide in AML patients that relapsed after, or were refractory to, high dose cytarabine (ara-C) containing regimens, in order to provide an alternative perspective.

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PATIENTS AND METHODS

Eligibility criteria. All patients were treated on protocols approved by the M. D. Anderson Cancer Center (MDACC) Institutional Review Board. Written informed consent was obtained from all participants according to institutional guidelines. Previously treated patients with relapsed- or refractory-AML with a first remission duration less than 1 year (or refusing salvage chemotherapy if longer) were eligible. In addition to exposure to prior ara-C containing-regimens, patients had to have a serum creatinine level ≤221 μmol/l, bilirubin level ≤42·75 μmol/l, Eastern

Co-operative Oncology Group performance status ≤3 and neither a seizure disorder nor other serious neurotoxicity prior to study entry. Because of the known teratogenic potential of thalidomide, patients who were pregnant or lactating were excluded, and participants of childbearing age were required to agree to use contraception methods during the study period and for 4 months after completion of therapy.

Therapy. Thalidomide (Celgene Corporation, Warren, NJ, USA) was provided as 50 mg gelatin capsules and given orally at bedtime at an initial daily dose of 200 mg. The daily dose was escalated by 200 mg each week as tolerated if no non-haematological toxicity greater than grade 1 was observed [graded according to the National Cancer Institute (NCI) Common Toxicity Criteria, version 2.0] up to a maximum of 800 mg daily. Therapy was continued for at least 2 months until lack of response, progressive disease, or unacceptable toxicity was observed.

Dose modifications were based on toxicity as follows: (1) grade 2 non-haematological toxicity persisting longer than 2 weeks resulted in dose reduction by one dose level; (2) if grades 3–4 non-haematological toxicity was observed, thalidomide was stopped until the toxicity was less than grade 2, and was resumed at a lower dose level if the patient was judged to be benefiting from therapy. A weekly to bimonthly dose reduced escalation schema of 50–100 mg increments was allowed if patients could not tolerate the 200 mg increments.

Evaluations. Baseline assessments (performed within 2 weeks of start of therapy) included a comprehensive medical history and physical examination; complete blood count with differential; sequential multiple analysis (SMA-12) including serum lactate dehydrogenase (LDH); and bone marrow aspirate with biopsy [to assess microvessel density (MVD) and cytogenetics if not recently performed within the previous 3 months]. Assessments for angiogenesis factors and marrow MVD were planned for 1, 3 and 6 months. Chest radiographs, electrocardiograms, and urinalysis were performed as clinically indicated. Haematological profiles and chemistries were usually obtained on an at least weekly basis and patients were assessed prior to dose escalation. The interval between assessments could be lengthened from every 2 weeks to every 3 months as indicated, depending on tolerance and response.

Criteria for response. All patients who had received at least one dose of thalidomide were considered evaluable for toxicity according to the NCI Common Toxicity Criteria. Those who received at least 14 d of thalidomide treatment were considered evaluable for response. Complete remission (CR) was defined as marrow blasts 5% or less in a normocellular or hypercellular bone marrow with neutrophil count $\geq 1 \times 10^9$/l and platelet count $\geq 100 \times 10^9$/l. Partial response (PR) was defined as a reduction of marrow leukaemia infiltrate (percent blasts × cellularity) to less than 20% with normalization of the granulocyte and platelet count as for CR.

Haematological improvement (HI) was defined as (1) ≥100% increase in neutrophil count to $\geq 1 \times 10^9$/l, (2) an increase in haemoglobin by ≥2 g/dl if below 10 g/dl, or a ≥50% decrease in packed red cell transfusion requirements, (3) ≥100% increase in platelet count to $>50 \times 10^9$/l if below that level prior to therapy, or (4) reduction in marrow blasts to 5% or less. Blasts were scored by morphological review of the marrows, with haematopathologists blinded to therapy. Response was also categorized by the response criteria used by Steins *et al* (2002), with PR defined as a ≥50% decrease in the marrow blast cell infiltration.

Statistical considerations. The study was designed to target patients with an expected CR rate of 10% or less (Estey *et al*, 1996). A two-stage design was implemented. If none of the first 14 patients treated had a response, the study was terminated; otherwise, an additional 11 patients could be entered to determine the response rate more precisely with a standard error ±10%.

RESULTS

Study group

A total of 16 patients were treated between September 1998 and December 1999 (Table I). Eleven (69%) had achieved a prior CR with ara-C-based chemotherapy. Their median first CR duration was 7 months (range, 1·5–25 months) (Table I). Five had failed to enter CR with one course of ara-C-based chemotherapy. Thalidomide was the first salvage attempt in seven patients, second in four, and third or greater in five.

A stratification system was developed by Estey *et al* (1996) to determine the probability of response to high dose ara-C-based salvage therapy based on duration of the first CR and the number of salvage attempts. Four groups were identified after analysis of outcome in a group of 206 patients with AML: (1) patients with initial CR duration greater than 2 years undergoing their first salvage attempt, (2) patients with an initial CR duration of 1–2 years who were not receiving their first salvage attempt, (3) patients with CR lasting less than 1 year, or (4) patients with no initial CR receiving second or subsequent salvage attempt without response to first salvage attempt.

The probabilities of achieving CR for each of these categories was 73% [95% confidence interval (CI), 45–92%], 47% (95% CI, 28–66%), 14% (95% CI, 8–21%), and 0% (95% CI, 0–4%) respectively. Based on their prior remission durations and number of salvage therapies received, one patient (6%) had a 40% probability of achieving CR with a high dose ara-C-containing salvage regimen, seven patients (44%) had a 10–20% probability, and eight patients (50%) had a less than 1% probability (Table I).

Response

One patient achieved marrow CR [6%, (95% CI 0·0–0·30)]. This patient had del(5)(q22q35) AML, and achieved a 4-month CR with induction high dose ara-C-based combination therapy followed by post-remission ara-C therapy. At relapse, 11% blasts were identified with mild anaemia (normal leucocyte and platelet counts). Blasts were associated with erythroid dysplasia and clearly aberrant myeloid

Table I. Characteristics and outcome after thalidomide in relapsed- or refractory-acute myeloid leukaemia (AML).

Patient no.	Age (years)	Duration first CR (weeks)	Number of prior salvages	Probability of response to standard therapy (%)*	Karyotype	Maximum dose of thalidomide (mg)	Duration therapy (d)	Response
1	73	32	1	<1	t(3;21)	800	91	PD
2	73	61	1	10–20	−7, −12	600	26	Death
3	36	107	4	<1	t(8;21),t(10;11)	800	35	PD
4	63	56	5	<1	t(15;15)	600	24	NR
5	68	0	0	10–20	t(1;7), +8	400	20	PD
6	76	0	1	<1	Diploid	800	72	NR
7	75	45	0	10–20	Ins(22;15)	800	43	PD
8	85	6	0	10–20	−5, add16q24, −17	800	61	HI (BM blasts 8% to 2%)
9	24	22	0	10–20	Diploid	200	12	PD
10	60	14	0	10–20	del(5)(q22q35)	600	94	CR
11	52	0	0	10–20	17q10	600	22	PD
12	65	0	1	<1	Diploid	700	45	NR
13	64	60	0	40	Diploid	400	11	PD
14	28	0	2	<1	Diploid	200	3	NR
15	59	12	2	<1	Diploid	600	28	NR
16	23	20	4	<1	t(11;19)(q23;p13)	400	21	HI (BM blasts 7% to 0%)

*Refer to Estey *et al* (1996).

HI, haematological improvement; NA, not applicable; PD, progressive disease requiring alternative therapy; NR, no response with therapy discontinued owing to lack of response or toxicity; BM, bone marrow; CR, complete remission.

Death in patient no. 2 related to pulmonary haemorrhage associated with thrombocytopenia.

phenotype by flow cytometry, and their presence was confirmed with three separate marrow aspirates about 1–2 weeks apart prior to study entry. The findings were consistent with relapse by consensus of the haematopathology group. After 38 d of thalidomide, the marrow blasts were reduced to 2%. Therapy was discontinued after 94 d because of persistent constipation and fatigue. The marrow response lasted for 36 months. Two additional patients had reductions in marrow blasts from 7% and 8%, to less than 5% in both cases. However, these reductions were transient, and were not accompanied by haematological recovery. Increase in marrow blasts was observed within 3–8 weeks whilst on therapy.

Drug delivery and toxicity

In three patients, dose escalation was not attempted because of progressive disease or toxicity. The remaining 13 patients (81%) received greater than 400 mg daily; however, dose escalation to 800 mg was possible in only five of the 13 (38%). The median daily dose was 400 mg. Three patients (19%) required dose reduction: reasons included fatigue, sedation, or neurotoxicity. The median duration of therapy was 27 d (range, 3–94 d), with seven patients discontinuing therapy because of progressive disease, four after failure to respond, two because of toxicity, and three owing to death. The latter group had not shown a response to thalidomide after 22, 26 and 72 d of therapy.

Angiogenesis assays

Levels of serum VEGF, bFGF, angiogenin, hepatocyte growth factor (HGF), and tumour necrosis factor-α (TNF-α) were measured prior to thalidomide in 15 patients using the methodology previously described (Aguayo *et al*, 2000). The median pretreatment level of VEGF was 33·89 pg/ml (range, 30·56–308·63), bFGF 6·14 pg/ml (range, 5·18–16·87), angiogenin 482 630 pg/ml (range, 231 060–656 960), HGF 771·6 pg/ml (range, 351·2–1922·4), and TNF-α 9·36 pg/ml (range, 8·63–12·48). These levels were not significantly different compared with controls (normal volunteers), except for HGF ($P = 0·002$ by t-test).

Serial cytokine assays were performed in six of the eight patients who remained on therapy longer than 30 d (as per study design), including two of the responders. The patient who achieved CR had an increase in VEGF levels (42·61–117·31 pg/ml), decrease in bFGF levels (16·87–7·3 pg/ml), and decrease in TNF-α levels (9·36–7·3 pg/ml). Patient number 8 had a decrease in VEGF (33·89–28·86 pg/ml) and bFGF (11·7–5·72 pg/ml), and increase in TNF-α (10·46–12·90 pg/ml). Decreases in VEGF and bFGF were also noted in three of the four non-responders.

DISCUSSION

In our study of single agent thalidomide, one of 16 (6%) patients with relapsed- or refractory-AML had a response as defined by standard criteria. Transient reductions in marrow blasts (HI) in two other patients were not clinically meaningful as they were not associated with haematological recovery. No significant correlations between pretreatment levels of angiogenesis factors or MVD and response were observed.

In contrast, Steins *et al* (2002) observed four partial responses and one HI among 20 patients with previously untreated- or relapsed-AML (response rate 25%, 95% CI, 8·6–49·1%), with responses maintained for a median of 3 months (range, 1–8 months). Decreases in plasma bFGF levels and marrow MVD correlated with response.

Applying the response criteria of Steins *et al* (2002) (i.e., 50% reduction in marrow blasts) to our group, three of the 16 patients (19%) treated in our study would have been categorized as responders, indicating that the response criteria used could account for disparities with regard to perception of significant clinical activity or lack thereof. Although there were presumed differences in patient selection, pretreatment characteristics, including marrow vascularity or levels of angiogenic factors, and duration of thalidomide treatment between the two studies, the most likely reason for the difference in observed response rates (6% vs. 25%) is the different response criteria used in each study (Table II). It is unlikely that small sample sizes account for the difference in response rates between our study (6%) and Steins *et al* (2002) (25%) given that the 95% CI for the difference in rates is −0·41, 0·03.

In a study of 83 patients with MDS treated with single thalidomide 100–400 mg/d, 16 patients (19%) had a HI, 10 of them becoming transfusion-independent (Raza *et al*, 2001). No complete responses were observed. Time to initial response was usually 12 weeks or greater. Patients with higher-risk disease [e.g. International Prognostic Scoring System (IPSS) intermediate-2 or higher] were significantly more likely to stop therapy early. Non-responders had higher pretreatment marrow blast counts and lower platelet counts than responders, suggesting that AML patients would also be less likely to respond to thalidomide therapy given the predominance of these features (Zorat *et al*, 2001).

In our study, all the patients were previously treated. Experience with thalidomide as a single agent in untreated AML is limited. Steins *et al* (2002) treated six patients with *de novo* AML, four with secondary AML and two older than 80 years of age. Karyotype was diploid in two and unknown in four patients. One diploid secondary AML had a PR. The other five patients discontinued therapy owing to progressive disease (two), failure to respond (one), toxicity (one) or personal reasons (one).

Our experience suggests that, used alone, thalidomide will not be an effective strategy for poor prognosis *de novo*, relapsed- or refractory-AML. Combination strategies with thalidomide and chemotherapy may be more promising, but a randomized study of liposomal daunorubicin and ara-C with or without thalidomide (400 mg daily escalated to 600 mg daily) in poor risk karyotype untreated AML did not demonstrate any prolongation in the duration of CR with the addition of thalidomide (Cortes *et al*, 2003). The planned combination was not feasible, as the majority of patients were not able to escalate the thalidomide dose as planned, or discontinued it owing to side-effects. Thus, the study may have been limited in its interpretation regarding

Table II. Summary of patient characteristics and response to thalidomide.

Characteristic	Category	MDACC (n = 16)	Steins *et al* (2002) (n = 20)
Number of responses	CR/PR/HI	1/–/2	–/4/1
Age (years)	Median (range)	64 (23–85)	69 (58–85)
Disease status (no.)	Untreated	–	6
	Relapsed/refractory	11/5	11/3
First CR duration (months)	Median (range)	7 (2–25)	15 (2–58)
No. of prior salvage treatments	0/1/≥2	7/4/5	Not reported
Karyotype (No.)	Diploid/unfavourable	6/10	5/8
	Not done	–	7
Thalidomide dose (mg/d)	Median (range)	400 (200–800)	200 (200–400)
Duration therapy (d)	Median (range)	27 (3–94)	49 (7–280)

CR, complete remission; PR, partial response; HI, haematological improvement; MDACC, M. D. Anderson Cancer Center.

efficacy, as the duration of therapy required for observed benefit may have been suboptimal.

Thalidomide analogues such as the Immunomodulatory Imide Drugs (ImiDs, Celgene Corporation) and Selective Cytokine Inhibitory Drugs (SelCIDs, Celgene Corporation) designed for increased efficacy and decreased toxicity (e.g. lack of teratogenicity or sedation) have been developed. These groups of analogues have distinct immunological effects although they both inhibit TNF-α production by activated monocytes/macrophages (Corral & Kaplan, 1999; Dredge *et al*, 2002). ImiDs inhibit TNF-α with a 10 000-fold increased potency compared with the parent compound, and resemble thalidomide in their ability to inhibit interleukin (IL)-1β, IL-6, and IL-12 while enhancing IL-10, IL-2, and interferon-γ. Co-stimulation of T cells is also significantly enhanced compared with thalidomide.

Phase I/II clinical trials of the ImiD CC-5013 have been conducted in MM and MDS (List *et al*, 2002a; Richardson *et al*, 2002). Reductions in paraprotenaemia were observed in 71% of 24 evaluable patients with previously treated MM, including those who had progressive disease after therapy with thalidomide (Richardson *et al*, 2002). Preliminary activity of CC-5013 (six of nine evaluable patients showed haematological responses) has been reported (List *et al*, 2002a). Dose limiting toxicity in both studies appeared to be myelosuppression (leucopenia and thrombocytopenia).

The sedation and neurotoxicity observed with thalidomide is often prohibitive in the generally older population of patients with AML. The more favourable toxicity profile (absence of constipation, sedation, or neuropathy) of CC-5013 compared with thalidomide may allow the prolonged administration needed to achieve the desired anti-angiogenic effect. In addition, *in vitro* data of CC-5013 in AML suggests that this agent may inhibit trophic response to VEGF and target inhibitors of receptor-mediated cytokine signalling (PI3-kinase/Akt-phosphorylation) (List *et al*, 2002b). With the biological activity of thalidomide observed in AML patients with low tumour burden, and the preliminary efficacy of CC-5013 in MM and MDS, investigation of thalidomide analogues (rather than the parent compound) as therapy for patients with AML is warranted.

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REFERENCES

Aguayo, A., Estey, E., Kantarjian, H., Mansouri, T., Gidel, C., Keating, M., Giles, F., Estrov, Z., Barlogie, B. & Albitar, M. (1999) Cellular vascular endothelial growth factor is a predictor of outcome in patients with acute myeloid leukemia. *Blood*, **94**, 3717–3721.

Aguayo, A., Kantarjian, H., Manshouri, T., Gidel, C., Estey, E., Thomas, D., Koller, C., Estrov, Z., O'Brien, S., Keating, M., Freireich, E. & Albitar, M. (2000) Angiogenesis in acute and chronic leukemias and myelodysplastic syndromes. *Blood*, **96**, 2240–2245.

Corral, L.G. & Kaplan, G. (1999) Immunomodulation by thalidomide and thalidomide analogues. *Annals of the Rheumatic Diseases*, **58**(Suppl 1), 107–113.

Cortes, J., Kantarjian, H., Albitar, M., Thomas, D., Faderl, S., Koller, C., Garcia-Manero, G., Giles, F., Andreeff, M., O'Brien, S., Keating, M. & Estey, E. (2003) A randomized trial of liposomal daunorubicin and cytarabine versus liposomal daunorubicin and topotecan with or without thalidomide as initial therapy for patients with poor prognosis acute myelogenous leukemia or myelodysplastic syndrome. *Cancer*, **97**, 1234–1241.

D'Amato, R.J., Loughnan, M.S., Flynn, E. & Folkman, J. (1994) Thalidomide is an inhibitor of angiogenesis. *Proceedings of the National Academy of Sciences of the United States of America*, **91**, 4082–4085.

Dredge, K., Marriott, J.B., Macdonald, C.D., Man, H.-W., Chen, R., Muller, G.W., Stirling, D. & Dalgleish, A.G. (2002) Novel thalidomide analogues display anti-angiogenic activity independently of immunomodulatory effects. *British Journal of Cancer*, **87**, 1166–1172.

Estey, E., Kornblau, S., Pierce, S., Kantarjian, H., Beran, M. & Keating, M. (1996) A stratification system for evaluating and selecting therapies in patients with relapsed or primary refractory acute myelogenous leukemia. *Blood*, **88**, 756.

Fiedler, W., Graeven, U., Ergun, S., Verago, S., Kilic, N., Stockschlader, M. & Hossfeld, D.K. (1997) Vascular endothelial growth factor, a possible paracrine growth factor in human acute myeloid leukemia. *Blood*, 89, 1870–1875.

Giles, F.J. (2001) The vascular endothelial growth factor (VEGF) signaling pathway: a therapeutic target in patients with hematologic malignancies. *Oncologist*, 6, 32–39.

Giles, F.J. (2002) The emerging role of angiogenesis inhibitors in hematologic malignancies. *Oncology (Huntingt)*, 16, 23–29.

Kenyon, B.M., Browne, F. & D'Amato, R.J. (1997) Effects of thalidomide and related metabolites in a mouse corneal model of neovascularization. *Experimental Eye Research*, 64, 971–978.

List, A.F., Kurtin, S.E., Glinsmann-Gibson, B.J., Bellamy, W.T., Buresh, A.J., Waddleton, D. & Knight, R. (2002a) High erythropoietic remitting activity of the immunomodulatory thalidomide analog, CC5013, in patients with myelodysplastic syndrome (MDS). *Blood*, 100(Suppl 1), 96a (abstr. 353).

List, A.F., Tate, W., Glinsmann-Gibson, B.J. & Baker, A. (2002b) The immunomodulatory thalidomide analog, CC5013, inhibits trophic response to VEGF in AML cells by abolishing cytokine-induced PI3-Kinase/Akt activation. *Blood*, 100(Suppl 1), 139a (abstr. 521).

Raza, A., Meyer, P., Dutt, D., Zorat, F., Lisak, L., Nascimben, F., du Randt, M., Kaspar, C., Goldberg, C., Loew, J., Dar, S., Gezer, S., Venugopal, P. & Zeldis, J. (2001) Thalidomide produces transfusion independence in long-standing refractory anemias of patients with myelodysplastic syndromes. *Blood*, 98, 958–965.

Richardson, P.G., Schlossman, R.L., Weller, E., Hideshima, T., Mitsiades, C., Davies, F., LeBlanc, R., Catley, L.P., Doss, D., Kelly, K., McKenney, M., Mechlowicz, J., Freeman, A., Deocampo, R., Rich, R., Ryoo, J.J., Chauhan, D., Balinski, K., Zeldis, J. & Anderson, K.C. (2002) Immunomodulatory drug CC-5013 overcomes drug resistance and is well tolerated in patients with relapsed multiple myeloma. *Blood*, 100, 3063–3067.

Singhal, S., Mehta, J., Desikan, R., Ayers, D., Roberson, P., Eddlemon, P., Munshi, N., Anaissie, E., Wilson, C., Dhodapkar, M., Zeddis, J. & Barlogie, B. (1999) Antitumor activity of thalidomide in refractory multiple myeloma. *New England Journal of Medicine*, 341, 1565–1571.

Steins, M.B., Padro, T., Bieker, R., Ruiz, S., Kropff, M., Kienast, J., Kessler, T., Buechner, T., Berdel, W.E. & Mesters, R.M. (2002) Efficacy and safety of thalidomide in patients with acute myeloid leukemia. *Blood*, 99, 834–839.

Thomas, D.A. & Kantarjian, H.M. (2000) Current role of thalidomide in cancer treatment. *Current Opinion in Oncology*, 12, 564–573.

Thomas, D.A., Giles, F.J., Cortes, J., Albitar, M. & Kantarjian, H.M. (2001) Antiangiogenic therapy in leukemia. *Acta Haematologica*, 106, 190–207.

Zorat, F., Shetty, V., Dutt, D., Lisak, L., Nascimben, F., Allampallam, K., Dar, S., York, A., Gezer, S., Venugopal, P. & Raza, A. (2001) The clinical and biological effects of thalidomide in patients with myelodysplastic syndromes. *British Journal of Haematology*, 115, 881–894.